



NDA 21-590/S-011

Beckloff Associates, Inc.
Attn: Gary Hindman, Ph.D.
Commerce Plaza II, Suite 300
7400 W. 110th Street
Overland Park, KS 66210

Dear Dr. Hindman:

We acknowledge receipt of your supplemental new drug application dated February 21, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for FazaClo (clozapine) Orally Disintegrating Tablets.

Reference is also made to an e-mail communications dated January 23, 2008 and June 26, 2008 from Dr. Sonny Saini, of this Agency, requesting labeling changes pertaining to acute dystonia, and informing you that these changes were class labeling changes for all antipsychotics.

We note in your email dated July 1, 2008 you agreed to the Agency's proposed language. We note your agreement to the language below.

Under **ADVERSE REACTIONS**, the addition of a new subsection entitled **Extrapyramidal Symptoms-Dystonia**

Class Effect: Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. Dystonic symptoms include: spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue. While these symptoms can occur at low doses, they occur more frequently and with greater severity with high potency and at higher doses of first generation antipsychotic drugs. An elevated risk of acute dystonia is observed in males and younger age groups. Clozapine, an atypical antipsychotic, is associated with a low incidence of dystonia [See Warnings, Tardive Dyskinesia].

Under **Warnings-Tardive Dyskinesia**, the revision of the sentence below.

There are several reasons for predicting that FazaClo may be different from other antipsychotic drugs in its potential for inducing tardive dyskinesia, including the preclinical finding that it has a relatively weak dopamine-blocking effect and the clinical finding of a low incidence of certain acute extrapyramidal symptoms, e.g., dystonia.

We have completed our review of this application, and it is approved, effective on the date of this letter with the above agreed upon language.

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/oc/datacouncil/spl.html>, that is identical in content to the above proposed changes to product labeling. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission “SPL for approved supplement NDA 21-590/S-011.”

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call LCDR Sonny Saini, Pharm. D., Senior Regulatory Project Manager, at (301) 796-0532.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Thomas Laughren
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